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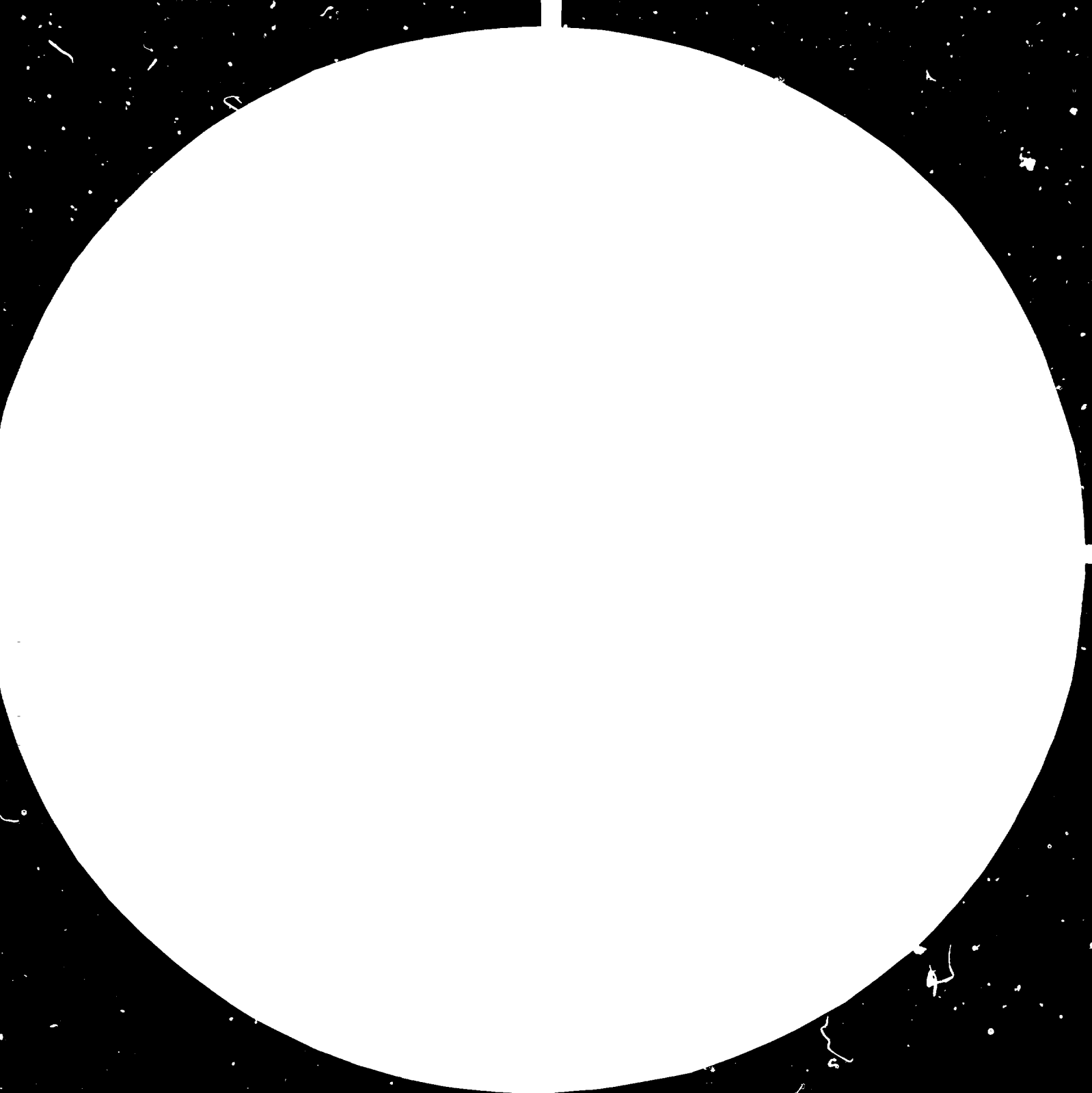

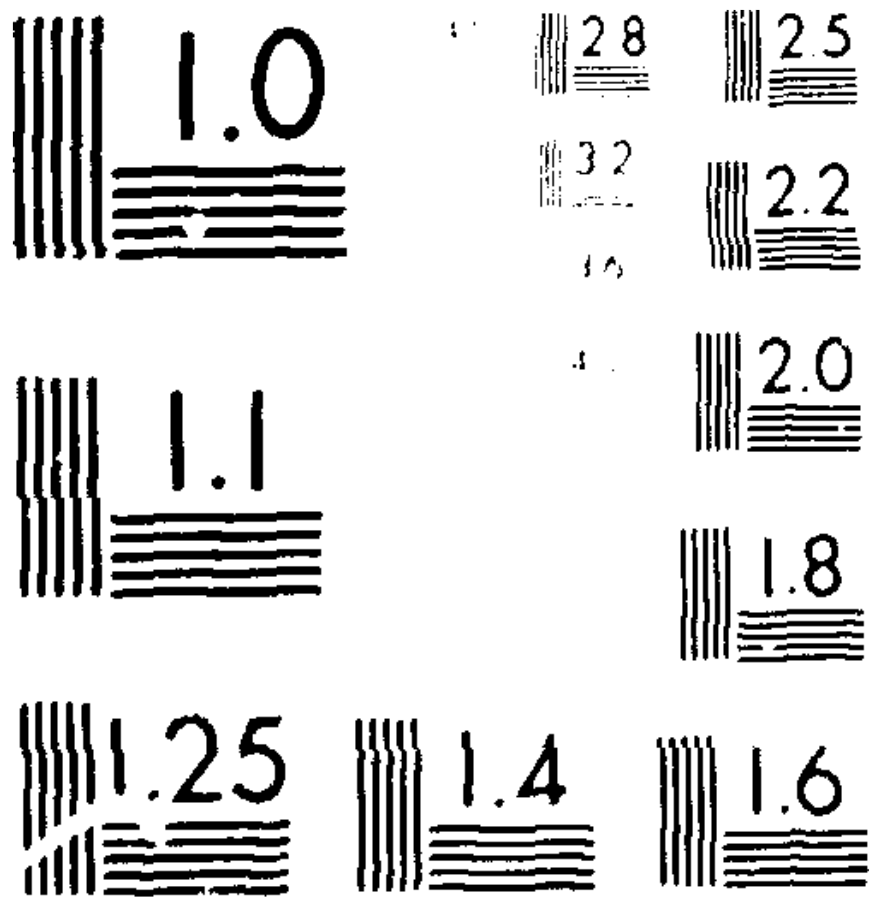
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THE AVAILABILITY, TERMS AND CONDITIONS FOR THE TRANSFER OF TECHNOLOGY FOR THE MANUFACTURE OF ESSENTIAL DRUGS*

Prepared by
the secretariat of UNIDO

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TABLES

I. INTRODUCTION

1. Developing countries are at various stages of development of the pharmaceutical industry ranging from simple formulation and packaging based on imported bulk drugs to the manufacture of bulk drugs based on local raw materials. 1/ The technology involved in the formulation and packaging of drugs is relatively simple. The manufacture of bulk drugs may be based on intermediate chemicals involving the last few steps of the process for the manufacture of the drugs concerned. The manufacture may also be based on raw materials, that is, bulk synthetic drugs or fermentation products such as antibiotics may be produced from basic chemicals, agricultural products, medicinal plants etc. The technology involved in the manufacture of bulk drugs is relatively more sophisticated than that involved in the formulation and packaging of drugs. Such a technology is available in developed countries, countries with centrally planned economies as well as in some of the developing countries.

2. For the purpose of integrated production of bulk drugs from intermediates or raw materials, 26 essential drugs have been identified by UNIDO and approved by WHO and these are shown in table 1. 2/ These drugs are widely used in the developing countries for treating diseases most prevalent in these countries. The developing countries also constitute large markets for many of these drugs. The production status of the 26 essential drugs in selected countries in Africa, Asia and Latin America based on UNIDO country studies is indicated in UNIDO Report. 3/ So far most of the technology transferred to the developing countries is for the formulation and packaging of drugs, where, as indicated earlier, the technology is relatively simple. There are just about seven developing countries which have some kind of base for the industrial scale production of some bulk drugs.

1/ Issues that might be considered at the First Consultation UNIDO/ID/WG.317/1

2/ op.cit. UNIDO/WG.317/1

3/ op.cit. UNIDO/WG.317/1

TABLE NO. 1

ILLUSTRATIVE LIST OF 26 ESSENTIAL DRUGS FOR WHICH FACILITIES FOR THE LOCAL MANUFACTURE OF ACTIVE INGREDIENTS SHOULD BE ESTABLISHED IN DEVELOPING COUNTRIES

ANALGESICS

1. Acetylsalicylic Acid
2. Paracetamol

ANTI-INFECTIVE DRUGS

Anthelmintic drugs

3. Mebendazole
4. Piperazine

Antibacterial drugs

5. Ampicillin
6. Benzyl Penicillin
7. Erythromycin
8. Sulphadimidine
9. Tetracycline

Antifilarial drugs

10. Diethylcarbamazine

Antileprosy drugs

11. Dapsone

Antimalarial drugs

12. Chloroquine
13. Primaquine

Antituberculosis drugs

14. Ethambutol
15. Isoniazid
16. Streptomycin

CARDIOVASCULAR DRUGS

Antihypertensive drugs

17. Hydralazine
18. Propranolol
19. Reserpine

DIURETICS

20. Furosemide

ANTI-DIABETICS

21. Insulin

ORAL CONTRACEPTIVES

22. Ethinylestradiol + levo-norgestrel

IMMUNOLOGICALS

23. Blood and blood fractions

VITAMINS

24. Ascorbic acid
25. Hydroxocobalamin
26. Retinol

II. IMPORTANCE OF AVAILABILITY OF TECHNOLOGY IN THE PHARMACEUTICAL INDUSTRY

3. A review of the present status of the development of the pharmaceutical industry in developing countries shows that the non-availability of technology for the manufacture of bulk drugs is perhaps the largest single constraint to the development of indigenous production of bulk drugs. It is observed that the developing countries experience considerable difficulty in obtaining access to suitable technology at a reasonable price. Where the developing countries have already secured technology for the manufacture of bulk drugs, such a technolgy was often based on the production of drugs from intermediates and not from raw materials.

4. Such limited technology transfer arrangements do not facilitate the development of an integrated pharmaceutical industry in the developing countries. First these countries hav to depend on the import of intermediates. Second the cost of imported intermediates is often so high in relation to the bulk drug cost as to render the local manufacture of bulk drugs uneconomic. 4/ Third the manufacture of drugs based on raw materials is most likely to render the manufacturing operations more viable. Last but not the least, many of the primary raw materials are available in the developing countries. For example, several of these countries have been the leading suppliers of medicinal plants used in the production of some essential drugs. Further some of the developing countries are in the process of establishing or expanding their petrochemical industry, which will make available many of the chemicals required by the drug industry.

5. The patents have expired in the case of most of the drugs under consideration. The drugs have been in existance for several years and it is understood that the expenditure incurred on research and development in the case of these drugs has already been recovered. The developing countries, therefore, feel that there is no longer any justification to withhold the transfer of technology to them.

6. In view of above, it is desirable that technology for the manufacture of essential bulk drugs should be made available to the developing countries. The availability of such a technology will facilitate the development in these countries of integrated pharmaceutical industry, which produces many of the bulk drugs required from local raw materials.

4/ op.cit. UNIDO/WG.317/1

III. AN ASSESSMENT ON THE AVAILABILITY OF TECHNOLOGY

7. Out of the 26 essential drugs identified by UNIDO and approved by WHO, UNIDO again selected nine drugs as priority for establishing facilities for the local production of bulk drugs and these are indicated in table 2. UNIDO carried out an indepth study of these drugs with particular reference to production, consumption and the situation regarding patents. 5/ The study revealed that the developing countries constitute large markets in the case of all these drugs. The primary raw materials required for the manufacture of these drugs are also available in some of the developing countries. However, it is observed that there is very limited ownership of the technologies to produce these drugs. Out of the essential drugs examined, the degree of penetration of technology in developing countries for Ampicillin and Tetracycline was maximum. This was mainly due to the fact that the technology for the manufacture of these two drugs became available to the developing countries from one of the developed countries. However, where the technology is held by few companies there has virtually been no transfer of technology to manufacture the bulk drugs based on raw materials to developing countries.

IV. REASONS GIVEN FOR NOT TRANSFERRING TECHNOLOGY

8. The reasons commonly given for not transferring technology are :

(a) large scale production is needed

(b) the required infrastructure is not available.

However, these are not always strictly valid as can be seen from the following case study relating to the antimalarial drug, Chloroquine Phosphate.

9. There are four major producers of Chloroquine Phosphate in the developed countries while 99 percent of the market for this drug is in the developing countries. One developing country has 33 percent of the world market for the antimalarial drug. In view of the prevalence of malaria on a very wide scale the developing country had to import over the years large quantities of Cloroquine Phosphate. WHO and UNICEF also donated appreciable quantities of the drug to supplement the imports by the Government. Yet the country's

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5/ The pricing and availability of intermediates and bulk drugs, UNIDO/ID/WG.331/4

TABLE NO. 2

ILLUSTRATIVE LIST OF 9 ESSENTIAL DRUGS FOR WHICH FACILITIES FOR THE LOCAL MANUFACTURE OF ACTIVE INGREDIENTS SHOULD BE ESTABLISHED IN DEVELOPING COUNTRIES AND WHICH SHOULD BE GIVEN TOP PRIORITY.

ANAGELSICS

1. Acetylsalicylic Acid

ANTI-INFECTIVE DRUGS

Antibacterial drugs

2. Ampicillin
3. Sulphadimidine
4. Tetracycline

Antifilarial drugs

5. Diethylcarbamazine

Antileprosy drugs

6. Dapsone

Antimalarial drugs

7. Chloroquine

Antituberculosis drugs

8. Ethambutol
9. Isoniazid

requirements of the drug could not be met with the result that large segments of the population could not have access to this drug. Since donation was no solution to this problem, the government was obliged to take up local production of Chloroquine Phosphate and decided to establish indigenous production based on raw materials instead of imported intermediates. The drug was of strategic value to the country and the infrastructure required to undertake the basic manufacture of the drug was available within the country.

10. The government then requested the subsidiary of transnational corporation to undertake the production from raw materials, but this did not materialize. Simultaneously, the government had been making efforts during the past six years to secure the technology for the manufacture of this drug from basic raw materials without any succes. In the intervening period malaria could not be effectively controlled due to non-availability of adequate quantities of the drug in time, since world production could not satisfy the demand as major producers of the drug curtailed production due to the introduction of new but more expensive antimalarial drugs. The government also approached UNIDO for assistance in securing such a technology. One holder was prepared to transfer technology for the production of Chloroquine Phosphate based on early intermediates under the auspices of UNIDO, but the transfer was linked to a commercial transaction and was, therefore, unacceptable. So far, UNIDO has been unable to secure technology for this drug in spite of the fact that economy of scale and infrastructure are available in the country. In the meantime, the developing country developed a laboratory process for the production of the drug on its own and is endeavouring to scale it up to commercial scale.

11. The above experience of the developing country shows that although the technology for the antimalarial drug is available in the developed countries and this drug is of great importance to the developing country which has large market and required infrastructure, the technology has not been made available to that country. Further some of the developed countries are using multi-purpose plants to produce a number of synthetic drugs in small volume and in such cases large scale production is not vital.

12. Furthermore, as tables 3 and 4 show, viable manufacturing units have been established with capacities ranging from 2 to 130 tons per year. This suggests that lack of large scale production cannot be the reason for not transferring technology.

TABLE NO. 3

Number of companies manufacturing nine essential drugs in different sectors and their capacity in a developing country.

	A	B	C
Acetylsalicylic Acid	1 (1,300)		
Ampicillin	3 (36)	1 (35)	
Chloroquine	2 (50)		1 (30)
Dapsone			1 (15)
Diethylcarbamazine		1 (15)	1 (15)
Ethambutol	3 (85)		
Isoniazid	3 (100)		1 (35)
Sulphadimidine		1 (600)	
Tetracycline	1 (30)	1 (90)	1 (10)

A National private sector
B National public sector
C Foreign firm

Figures within brackets indicate total capacity in metric tons.

TABLE NO. 4

Small Scale units producing bulk drugs in a developing country and the range of their capacity

SNO	Item	Annual capacity (in kg or metric tons)	No. of units	Minimum annual capacity	Maximum annual capacity	Remarks
1	Chloramphenicol powder	kg	4	2,000	5,000	3 units produce from Levo base. 1 unit from S-base
2	Sulphamethoxazole	kg	2	2,000	15,000	From imported isoxamine
3.	Vitamin B1 (non-parenteral)	kg	1	na	12,000,	From imported Utriothiamine
4	Niacinamide	M/T	2	12	25	From bought gamma picoline
5	Oxyphen Butazone	M/T	4	2	20	
6	Paracetamol	M/T	5	6	7,100	
7	Phenyl Butazone	M/T	1		20	
8	Analgin	M/T	4	7	150	
9	Isoniazid	M/T	3	3	35	
10	Metronidazole	M/T	1		5	
11	Diiodohydroxy quinoline	M/T	3	2	28	
12	Iodochlorohydroxy quinoline	M/T	1		12	
13	Piperazine Citrate	M/T	1		6	From Piperazine Anhydrous

V. TECHNOLOGY RELATING TO DRUGS PRODUCED FROM MEDICINAL PLANTS

13. The situation with regard to drugs produced from medicinal plants illustrates how the developing countries cannot obtain access to the technology held by a few companies in the developed countries. Many of the developing countries have rich flora of medicinal herbs and plants and have been the leading suppliers of medicinal plants. They have been the sole producers and exporters of a number of plants that do not occur elsewhere. The developed countries have been the major importers and users of the medicinal plants. According to an estimate, 25 percent of all the prescriptions issued in the USA every year contain one or more drugs from plants and the American public pays more than 3 billion US$ for the cost of the drugs solely derived from plants (calculated on the over the counter price). A number of essential drugs used in modern medicine can be produced from medicinal plants. 6/ The WHO list of essential drugs includes over 30 drugs of plant origin. 7/

14. The value of imports of plant seeds, flowers and parts of the plant primarily used in perfumery, pharmacy or for insecticidal or fungicidal prupose, etc. into OECD countries had increased from US$ 52.9 million in 1967 to US$ 217 million in 1976. 8/

15. The developed countries process the medicinal plants into alkaloids hormones, etc., whereby the value of the export of the items increases as much as tenfold. Switzerland offers an illustrative example. In 1976 the imports of medicinal plants accounted for US$ 5.1 million and alkaloids for US$ 9.7 million, with a total of US$ 14.8 million, whereas the export of medcinal plants was US$ 1.6 million and alkaloids US$ 162.3 million, totalling US$ 164.4 million - a tenfold increase. The combined exports of derivatives/active principles of medicinal plants by the six countries UK, USA, West Germany, France, Switzerland and Japan totalled US$ 752.5 million, the major exporter being West Germany with US$ 251.5 million, followed by Switzerland with US$ 207.8 million and the USA with US$ 140.7 million. The major item of export was alkaloids valued at US$ 324.6 million, followed by hormones with US$ 234.4 million and vegetable saps/extracts amounting to US$ 119 million. Switzerland was the largest exporter of any single

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6/ Report of the Technical Consultation on Production of Drugs from Medicinal Plants in Developing Countries; UNIDO, ID/WG. 271/

7/ The Selection of Essential Drugs, WHO Technical Report Series 641, 1979

8/ Seminar on export potential, Export Promotion Council, India, 1980

group of items mentioned above, her exports in respect of alkaloids being US$ 162.8 million. Hungary and other countries with centrally planned economies also import medicinal plants of considerable value although accurate figues are not available.

16. Although some developing countries are sole producers of medicinal plants, the countries export the medicinal plants to the developed countries, because they do not have access to the technology. Clearly international co-operation is lacking in this vital field.

17. Institutes for the purpose of screening medicinal plants are available in some developing countries. The UN organizations assisted in establishing some of these. Whenever some potentially useful medicinal plant is found, it is stated that the developed countries import these plants for processing instead of transferring technology to the concerned developing country. Thereby, the developing countries continue to be the exporters of medicinal plants instead of deriving benefit from the establishment of pharmaceutical industry based on medicinal plants.

VI. METHODOLOGY FOR TRANSFER OF TECHNOLOGY

18. Different methods for the transfer of technology are described in UNIDO Report.[9/] The following methods are widely used:

1. Establishment of subsidiaries by foreign companies
2. Joint ventures
3. Transfer of technology under license
4. Sale of technology

9/ Second Panel Meeting of INdustrial Experts on the Pharmaceutical Industry, UNIDO, ID/WG. 267/4/Rev. 1

19. The establishment of joint ventures or subsidiaries of foreign companies facilitated to some extent the acquisition of suitable technology. However, according to some developing countries, most of such arrangements involve merely the formulation and packaging of drugs, where the technology is relatively simple. It is observed that in some developing countries the governments had to pass regulations to force the foreign companies to establish facilities for the manufacture of bulk drugs being formulated. It is stated that even then the foreign companies often based their manufacture on late intermediates and not on raw materials.

20. The establishment of joint ventures is desirable in the case of manufacture of bulk drugs subject to the following conditions:

- technology should preferably be based on raw materials
- equity participation by the foreign company in cash instead of in kind
- possibility to export
- compulsory transmission of innovations
- freedom to purchase intermediates, raw materials and equipment from any suitable source.

It is believed that this could be one of the best methods for the transfer of technology.

VII. ALTERNATIVE SOURCES OF SUPPLY OF TECHNOLOGY

21. The technology for the manufacture of some essentail drugs is available with countries with centrally planned exonomies. For example, out of the seven drugs, technology for semi-synthetic Penicillin, Isoniazid, Ethambutol and Chloroquine Diphosphate is available in some of these countries.[10/] The technology for the manufacture of nine essential drugs is also available in some developing countries, although the technologies are based on early or late intermediates in most of the cases. To this extent, the other developing countries wishing to establish facilities to manufacture these bulk drugs consider this alternative source of supply for the technology.

10/ Pharmaceutical Meeting on the Production of Essential Drugs in Developing Countries, UNIDO/IOD/336

VIII. ANALYSIS

22. Access to technology for bulk drug production at a reasonable price is a major constraint on the development of an integrated pharmaceutical industry in developing countries. It is observed that the technology made available so far has often been based on the use of imported intermediates in the manufacturing process and the high cost of intermediates frequently renders local production of the bulk drug uneconomic. The technology based on the use of raw materials is most likely to render the manufacturing operations viable.

23. Developing countries are large consumers of many essential drugs, which are needed to treat diseases widely prevalent in these countries. In view of this, these countries should have access to the technology to manufacture such drugs.

24. Many raw materials required for the production of essential drugs are available in some developing countries. In the case of medicinal plants, the developing countries are the sole producers of some plants. Hence the technology to process these plants in order to derive much higher value from their resources should be made available. Similarly the developing countries should have access to the technology for the production of drugs based on local raw materials. It is to be assumed that there will be better co-operation between the developed and developing countries to facilitate the transfer of such a technology.

25. The technology for the production of some of the essential drugs is also available in some developing countries. This could be an alternative source for the supply of technology and one, therefore, need not always look to the traditional sources of technology.

26. The developing countries need to strengthen their research and development base to develop their own technology, as for example, in the field of medicinal plants. Although this process will take some time to materialize the developing countries need to become more independent in the field of technology in this vital industry.

27. Means to achieve the above objectives should be discussed at the First Consultation.